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Stereoselectivity in bis-1 (2-Pyridyl) ethylaminecobalt (III)

Richard Lindsay Wellman
Union College - Schenectady, NY

Stereoselectivity

in

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ABSTRACT

Recently Michelsen reported the synthesis of a new series of bis-chelated cobalt(III) compounds using 2-pyridylmethylamine (pm) as a bidentate ligand.[4] Replacement of a methylene hydrogen of pm with a methyl group gives the optically active compound 1-(2-pyridyl)ethylamine (pa). Model studies show that when bound to a cobalt molecule, the ligand methyl group can assume either an axial or an equatorial position. On the basis of predictions by Corey and Bailar[1] using the ligand 1,2-diaminopropane, it was thought stereoselectivity might be observed in the reaction of pa with cobalt. To determine if this was so, Michelsen's reactions were carried out using the pa ligand in both the racemic form and in the resolved form. The products were chromatographed to determine relative amounts of products. On the basis of relative intensities of the spots, it was concluded stereoselectivity did occur, but it was impossible to determine which isomer was favored.

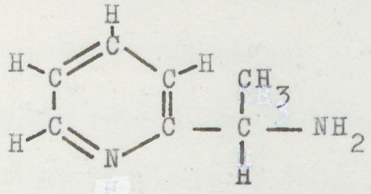
I would like to thank Professor Charles Weick for making this research not only an instructive experience but an enjoyable one as well.

Richard L. Wellman

TABLE OF CONTENTS

INTRODUCTION

Stereoselectivity is the preference of a specific ligand conformation for a given metal configuration. This subject has been under study for some years and has been fairly well characterized for complexes containing 1,2-diamines. This paper moves slightly away from the diamine trend by employing 1-(2-pyridyl)ethylamine (pa)(Figure 1) as the ligand in a series



p a

Figure 1. 1-(2-Pyridyl)ethylamine

of reactions hoping to find evidence of stereoselectivity in the products.

The absolute configurations of ethylenediamine (en) cobalt (III) complexes take the two enantiomeric forms shown in Figure 2. The two methods of distinguishing the enantiomers

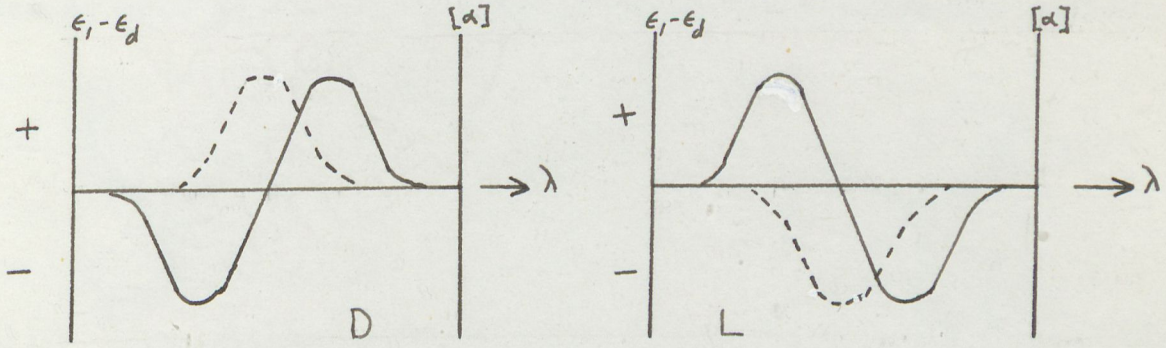
C_2- D C_3- Λ C_3- Δ C_2- L

Figure 2. Configurations of cobalt(III) complexes

consider the C_2 and C_3 symmetry axes. A right-helical rotation about the C_2 or a left-helical rotation about the C_3 indicate the D or Λ form, while left-helical rotation about the C_2 or right-helical rotation about the C_3 give the L or Δ absolute configuration. Being enantiomers, these isomers are chemically

indistinguishable and cannot be separated by other than resolution using some asymmetric technique. Once separated, however, they can be identified on the basis of their optical rotary dispersion (ORD) and circular dichroism (CD) curves.

A beam of plane polarized light can be resolved into two circularly polarized beams, one with a right rotation and the other with a left rotation. A stereo isomer of an optically active complex has a difference in refractive index for the left and right polarized beams which causes a retarding of one polarized component relative to the other resulting in a rotation of the plane of light. A plot of this rotation vs. wavelength gives an ORD curve (Figure 3). Closely related to the



— = ORD; --- = CD

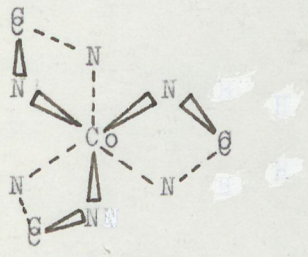
Figure 3. Cotton effect in ORD and CD spectra

refractive index of a molecule is its molar absorbtivity, ϵ. Since the refractive index for the right and left polarized beams is different, a difference $\epsilon_l - \epsilon_d$ should be observed. Indeed, if a plot of $\epsilon_l - \epsilon_d$ vs. wavelength is made, the CD curve in Figure 3 results. The characteristic shapes of the ORD and CD curves are labeled the Cotton effect. The Cotton effect is designated + or - depending on the position of the high wave-

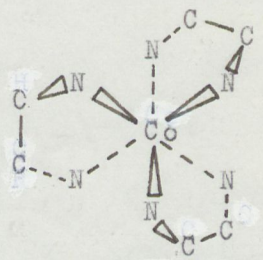
length lobe on ORD, and the position of the single lobe in CD.

It should be pointed out, however, that the curves shown in Figure 3 are for an isolated electronic transition and are generally much simpler than anything found experimentally. Often what an experimenter finds is a succession of maxima and minima (a Cotton effect for each transition) bearing only slight resemblance to the idealized curves of Figure 3. Even in these difficult cases though it has been possible to correlate the absolute configurations with the sighs of the Cotton effects for the various transitions.

Not only does $[Co(en)_3]^{3+}$ have two absolute configurations, but each ligand itself has two conformations about the metal atom as seen in Figure 4. Note that in one complex the carbon-



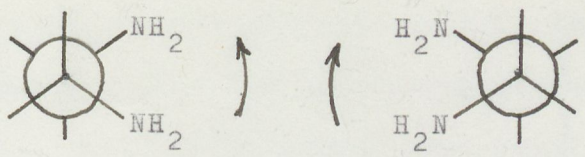
"lel"



"ob"

Figure 4. Ethylenediamine "lel" and "ob" conformations.

carbon bond of en is parallel to the C_3 axis ("lel" conformer), and in the other is perpendicular ("ob" conformer). Corey and Bailar[1] calculated the energy differences on the basis of hydrogen repulsions of the two complexes and found the "lel" form favored by 1.8 kcal $mole^{-1}$. The two conformations in Figure 4 correspond to a right-handed helix about the en carbon-carbon bond (k conformer) and a left-handed helix (k' conformer) which are diagrammed in Figure 5. The relationship of the



k' k

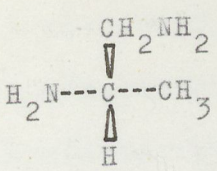
Figure 5. Configurations of k and k' ethylenediamine.

D "lel" to the L "lel" form is shown in Figure 6. Note that

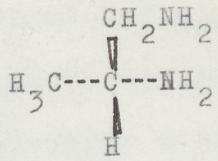
D(kkk) "lel" L(k'k'k') "ob"

Figure 6. D "lel" and L "lel" ethylenediamine conformations. for D configurations the "lel" conformation is the result of k conformation ligands while the "lel" L conformations are found using k' conformers. Inspection shows that the D(kkk) and L(k'k'k') are enantiomers and equally favored. Least favored are the enantiomers D(k'k'k') and L(kkk) which both have "ob" conformations. The diastereomers D(kkk') and D(kk'k') are found to be between the tris "lel" and tris "ob" conformers in energy.

Replacing a methylene hydrogen in en with a methyl group gives 1,2-diaminopropane (pn) which is an optically active ligand. In Figure 7 the absolute configurations of the dextrorotatory (+) and levorotatory (-) isomers are shown. For this ligand Corey and Bailar[1] found that not only did the "lel" and "ob" distinction exist but that the methyl group could be either axial or equatorial when the ligand was bound to the metal atom.



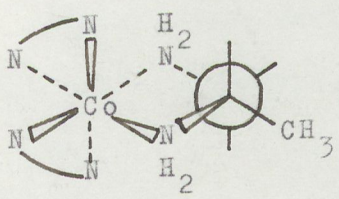
(+)pn



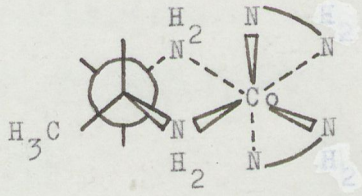
(-)pn

Figure 7. Absolute configurations of 1,2-diaminopropane

They calculated that the conformations possessing methyl groups in an equatorial position were 2 kcal mole^{-1} more stable than conformations with methyl groups in an axial position which assures that only ligands with equatorial methyl groups will be found in the "ob" and "lel" conformations of the ligands. Looking at Figure 8 it is obvious that k conformations correspond to (+)pm and k' conformations correspond to (-)pn.



D(kkk) ≡ D(+++)



L(k'k'k') ≡ L(---)

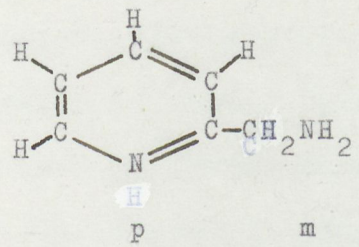
Figure 8. Relationship of conformation to absolute configuration of 1,2-diaminopropane.

Applying what we found for $[Co(en)_3]^{3+}$ we would expect to find preferential formation of the enantiomers D(+++) and L(---), both of which are the "lel" conformers, with lower yields of D(---) and L(+++). Dwyer, Sargeson and James[2] actually separated the products of the reaction of cobalt and (±)pn, finding these predictions to be true. Equilibrium amounts of these products also showed Corey and Bailar's energy calculations to be very close to the truth.

The energy differences discussed above for tris-diamine

cobalt(III) complexes should also be correct for bis- chelated cobalt(III) complexes, the only difference being that the energy separations between "lel" and "ob" forms will be reduced by one third.[3,4] One would still expect to see preferential formation of "lel" over "ob" complexes.

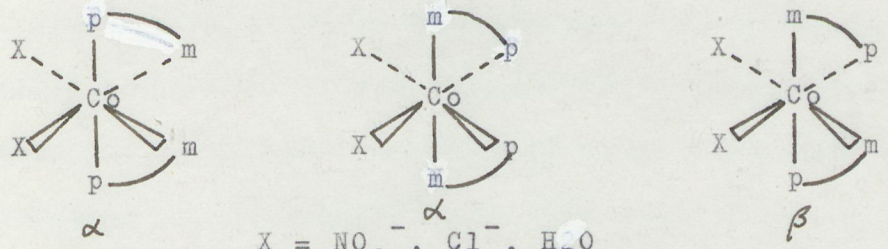
In recent work by Michelsen[3] some new chelated cobalt(III) complexes using the ligand 2-pyridylmethylamine (pm) (Figure 9) were isolated.[4] This worker used two reaction schemes to get



p m

Figure 9. 2-Pyridylmethylamine

two series of products named α and β seen in Figure 10.



α α β

$X = NO_2^-, Cl^-, H_2O$

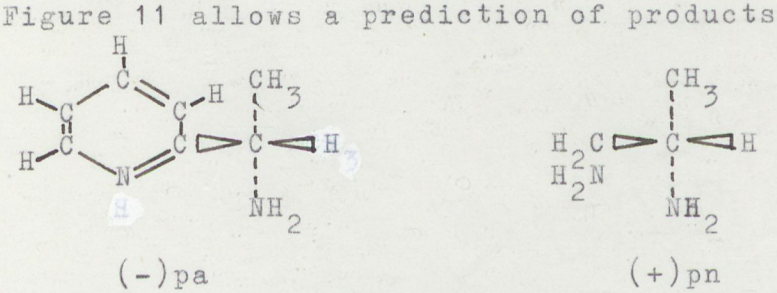
Figure 10. α and β isomers of $[Co(pm)_2X_2]$

In the α series either the pyridyl nitrogens are trans with all other groups cis or the amine proups are trans with all other groups cis. In the α series Michelsen was unable to say whether the amine or pyridyl nitrogens were trans. There appears no reason both isomers are not present as molecular models show no obvious steric reasons for one isomer's predominance over another. Both the α and β forms are characterized by their NMR spectra. As the β form lacks the C_2 axis of symmetry

found in the α forms, the corresponding ligand hydrogens have slightly different shifts which cause the NMR spectrum to appear very complicated. The α form has a very pure spectrum and does not show the same complications.

Replacement of a methylene hydrogen in pm by a methyl group gives the optically active compound 1-(2-pyridyl)ethylamine (pa) seen in Figure 1. If bound to a metal atom one might expect to see some stereoselectivity in the reactions. The ligand is of additional interest in that it is a slight step away from the previously used 1,2-diamines, and there has been little work done with pyridine amines in any aspect of inorganic chemistry. The ligand is slightly constrained in a planar form by the sp^2 bonding of the pyridine ring, so less differentiation between the "ob" and "lel" conformations is likely. Despite this, model studies show the methyl group can assume well-defined axial and equatorial positions for the two conformations. Work with alanine has also shown that despite the sp^2 bonding, stereoselectivity does occur.[5]

The correlation of the absolute configurations of pa and pn in Figure 11 allows a prediction of products on the basis



(-)pa (+)pn

Figure 11. Absolute configurations of (-)pa and (+)pn

of the similarity of (+)pn to (-)pa. Corresponding to the pn series we assign the k conformer to (-)pa and the k' conformer

to (+)pa. If the results of the stereoselectivity outlined for en and pn hold for pa then the reaction products will show larger yields of the D(--) and L(++) enantiomers in relation to the amounts of D(++) and L(--). Paper chromatography of reaction products should show (for the D absolute configuration) the isomers D(--), D(+-), and D(++) in order of decreasing yield, with of course the corresponding enantiomers of the L configuration. CD and ORD spectra of the predominant compounds should verify the assumptions made if the resolved ligand is used thus allowing formation of only two enantiomers.

In the present work two separate reaction series were carried out. The products of cobalt's reaction with the racemic ligand and the levorotatory form of the resolved ligand were chromatographed in the hopes of observing separation of the products mentioned above. Both the chloro and aquo products of the β isomer were used. The α product was not chromatographed due to the possibility of the two geometrical isomers confusing the results, but it was prepared in order to complete Michelsen's reaction series with the pa ligand.

EXPERIMENTAL

Materials: All chemicals used for synthesis were of reagent purity.

1-(2-pyridyl)ethylamine: The pyridyl amine was synthesized following Smith and Rajevsky.[6] To 63.0 g of 99% formamide at 160-180° was added dropwise over a half-hour with stirring, 12.1 g of 2-acetylpyridine in 15 ml of 98% formic acid. When addition was complete an additional 15 ml of formic acid was added and the mixture was heated at 160-180° for an additional 1.5 hours. After cooling and pouring into 100 ml of water, the solution was made alkaline to pH 11 with conc. sodium hydroxide. The solution was thoroughly extracted with ether, and the ether was dried over sodium sulfate. Flash evaporation of the ether yielded from 7 to 11 g of impure intermediate.

The intermediate was heated with 6 ml of 8.5 M hydrochloric acid per gram of impure intermediate at 160-180° for 5 hours. The cooled solution was made alkaline to pH 11 with conc. sodium hydroxide. The solution was extracted thoroughly with ether, and the ethereal solution was dried over sodium sulfate. The ether was evaporated and the residue was distilled under aspirator pressure (16-20 Torr) to give the colorless amine boiling at 84-88° in amounts ranging from 6.5 to 10.0 g. Yield: 50-80%.

(-)-1-(2-pyridyl)ethylamine: Resolution of the amine followed Smith et. al.[7] To 10.0 g of (±)-1-(2-pyridyl)ethylamine in 150 ml of boiling 95% ethanol were added 15.0 g of (+)-tartaric acid in 150 ml of boiling 95% ethanol. On cooling, white crystals formed. These were recrystallized to white

needles with mp 159-162°. Yield was 3.4 g (30%). Decomposition of 12 g of the amine-tartrate salt in aqueous sodium hydroxide, collection of the amine in ether, drying of the ethereal solution over sodium sulfate, evaporation of the solvent, and distillation under aspirator pressure gave 2.7 g (51%) of (-)-1-(2-pyridyl)ethylamine, bp 84-90°, $[\alpha]_D^{20} = -31.4$ (c 5.32 absolute ethanol).

α-$[Co(pa)_2(NO_2)_2]NO_2$: 2.0 g of sodium cobaltinitrite were dissolved in 2 ml of water. To this was added dropwise with stirring, over a 15 minute period, a solution of 1.2 g (-)pa or (±)pa in 5 ml of water. A bulky red-orange precipitate formed and slowly gave way to a yellow precipitate. After cooling on ice the yellow precipitate was filtered and recrystallized by dissolving in boiling water and then cooling on ice. Yields: α-$[Co(\pm)pa_2(NO_2)]NO_2$, 0.40 g, 18%; α-$[Co(-)pa_2(NO_2)_2]NO_2$, 0.45 g, 20%.

α-$[Co(pa)_2Cl_2]Cl$: 0.40 g of α-$[Co(pa)_2(NO_2)_2]NO_2$, containing either (±)pa or (-)pa were suspended in a few ml of 3 M hydrochloric acid. A few ml of 8% lithium chloride in 95% ethanol were added, and the solution was heated in a boiling water bath. The solution slowly changed a purple- dark blue color. Evaporation to dryness gave a purple solid. Some green crystals (presumed trans-chloro product) were observed. Washing of the solid with 95% ethanol removed most of these. Recrystallization of the product was achieved by dissolving the purple solid in boiling water followed by cooling on ice, giving purple crystals. Addition of small amounts of the same 8% lithium

chloride solution was found to aid recrystallization. Yield: α-$[Co(pa)_2Cl_2]Cl$ containing either (-)pa or (±)pa, 0.29 g, 78%.

α-$[Co(pa)_2(H_2O)_2]^{3+}$: 0.29 g of α-$[Co(pa)_2Cl_2]Cl$ containing either (-)pa or (±)pa was added to a warm solution of 0.44 g silver nitrate in 5 ml of water. Filtration of the silver chloride formed left a pinkish solution from which it was impossible to isolate crystals.

β-$[Co(pa)_2(NO_2)_2]NO_2$: 2.9 g of cobalt(II) nitrate hexahydrate and 1.5 g of sodium nitrite were dissolved in 10 ml of water. An ice-cooled mixture of 2.4 g (-)pa or (±)pa and 1 ml of conc. nitric acid was added, and the solution was oxidized either by drawing a stream of air through it for an hour, or by addition of 30% hydrogen peroxide. The brown-yellow precipitate was filtered and washed with ice-water and acetone. The product was recrystallized from boiling water to give yellow crystals. Yields: β-$[Co(\pm)pa_2(NO_2)_2]NO_2$, 0.8 g, 18%; β-$[Co(-)pa_2(NO_2)_2]NO_2$, 0.7 g, 16%.

β-$[Co(pa)_2Cl_2]Cl$: 0.42 g of β-$[Co(pa)_2(NO_2)_2]NO_2$ containing either (-)pa or (±)pa was suspended in a few ml of conc. hydrochloric acid and the solution heated in a boiling water bath until it had turned a deep bluish-purple. The solution was evaporated to dryness. After washing with acetone and ethanol the solid was recrystallized from boiling water to give purple crystals. Crystallization was facilitated by addition of 8% lithium chloride in 95% ethanol. Yield: 0.31 g, 73%.

β-$[Co(pa)_2(H_2O)_2]^{3+}$: 0.35 g of β-$[Co(pa)_2Cl_2]Cl$ containing

either (-)pa or (±)pa was added to a hot solution of 0.53 g of silver nitrate in 5 ml of water. The solution was filtered from the precipitated silver chloride, leaving a pinkish liquid. It was impossible to induce crystallization.

Chromatography: The β-aquo and β-chloro isomers were chromatographed on Whatman Grade 1 Chromatography Paper using butanol saturated with hydrochloric acid as the moving phase. R_f values were calculated as the ratio of the distance moved by the compound to the distance moved by the solvent.

Spectra: UV-visible spectra were run on Union College's Perkin Elmer PE202. NMR spectra were run on the college's Hitachi-Perkin Elmer R24A.

RESULTS AND DISCUSSION

Synthesis: The pyridylamine synthesis was straightforward. The NMR shows the expected peaks with appropriate chemical shifts (Appendix 1). Boiling points were the same as literature values after allowing for the differences in vacuum during the distillation. Yields tended to decrease as time went on due probably to polymerization of the formic acid.

The cobalt complexes were prepared following Michelsen's methods for 2-pyridylmethylamine.[4] The nitro cobalt complexes crystallized well, the chloro compounds crystallized fairly well, and the aquo complexes did not crystallize at all. NMR of the β-aquo complexes (Appendix 1) showed the expected complicated splitting patterns when compared to the ligand NMR. The absorption band for water unfortunately lay directly over the methylene hydrogen peaks and could not be moved by trifluoroacetic acid, so comparisons for that group could not be made. The α-aquo compound was so impure no NMR could be made although UV-visible spectra were useful. In Table 1 are tabulated the spectral data

Table 1. Wavelengths (nm) of maximum absorbance for bis-1-(2-Pyridyl)ethylaminecobalt(III).

Compound	pm	(±)pa	(-)pa
α-$[Co(pa)_2(NO_2)_2]NO_2$	438.5	438	
α-$[Co(pa)_2Cl_2]Cl$	538.5	505	
α-$[Co(pa)_2(H_2O)_2]^{3+}$	353, 489	348, 487	
β-$[Co(pa)_2(NO_2)_2]NO_2$	444	438	441
β-$[Co(pa)_2Cl_2]Cl$	534	533	508
β-$[Co(pa)_2(H_2O)_2]^{3+}$	353, 489	357, 486	356, 486

found. With the exception of the two chloro products

α-[Co(±)pa_2Cl_2]Cl and β-[Co(-)pa_2Cl_2]Cl, all wavelengths of maximum absorbance are very close to Michelsen's.[4] The only way to explain the departure of the two chloro compounds from Michelsen's data is to assume there were impurities in the compounds. These spectra were run on samples which had not yet been recrystallized so some other chloro and possibly nitro products might have been in solution. Looking at the UV spectra for the aquo complexes (Appendix 1), the same absorbance differences in the 350 nm region observed in Michelsen's spectra are seen. This gives further evidence that both the α and β series were prepared. All the spectral comparisons for compound identification assume that the addition of a methyl group will not change the bonding characteristics of the ligand. Obviously the assumption is a good one judging by the correlation between the pn and pa maximum absorbances as well as the differences in curve shape for the aquo complexes.

The addition of the methyl group to the ligand can possibly account for the marked decrease in yields (one-half those reported by Michelsen[4]). The increased steric hindrance of the methyl group probably prevents the easy formation of the complex.

Chromatography: For the β products of the reaction with the racemic ligand, three spots are observed with the R_f values and relative intensities shown in Table 2. The products would be the D(--), D(+-), and D(++) diastereomers accompanied by their respective enantiomers L(++), L(+-), and L(--). The enantiomers, being inseparable, appear in the same spot on the

Table 2. R_f values and relative intensities of chromatographed complexes.

compound	R_{f1}, intensity	R_{f2}, intensity	R_{f3}, intensity
β-$[Co(\pm)pa_2(H_2O)_2]^{3+}$	0.96, M	0.14, H	0.039, L
β-$[Co(-)pa_2(H_2O)_2]^{3+}$		0.20, H	0.079, L
β-$[Co(-)pa_2Cl_2]^{+}$		0.17, L	0.043, H

Intensities: H = high, M = medium, L = low.

paper. Some insight as to the identities of the various spots can be gained by comparison with the results obtained by chromatographing the aquo products from the reaction of the resolved levorotatory ligand. Although a clear separation was not obtained, only two spots with the R_f values and relative intensities shown in Table 2 were observed. These products should be the D(--) and L(--) diastereomers. The higher intensity band seems to be the one with R_f = 0.20, and the difference in intensity suggests a preference for this isomer. Since the D(--) isomer has the "lel" conformation, and L(--) isomer has the "ob" conformation, the D(--) isomer should be the major product. On this basis the spot with R_f = 0.20 can be assigned to the D(--) isomer while the spot at R_f = 0.079 should be the L(--) isomer. The absence of the third dot indicates that the spot with R_f = 0.96 in the β-$[Co(\pm)pa_2(H_2O)_2]^{3+}$ chromatogram is due to the D(+-) and L(+-) isomeric pairs.

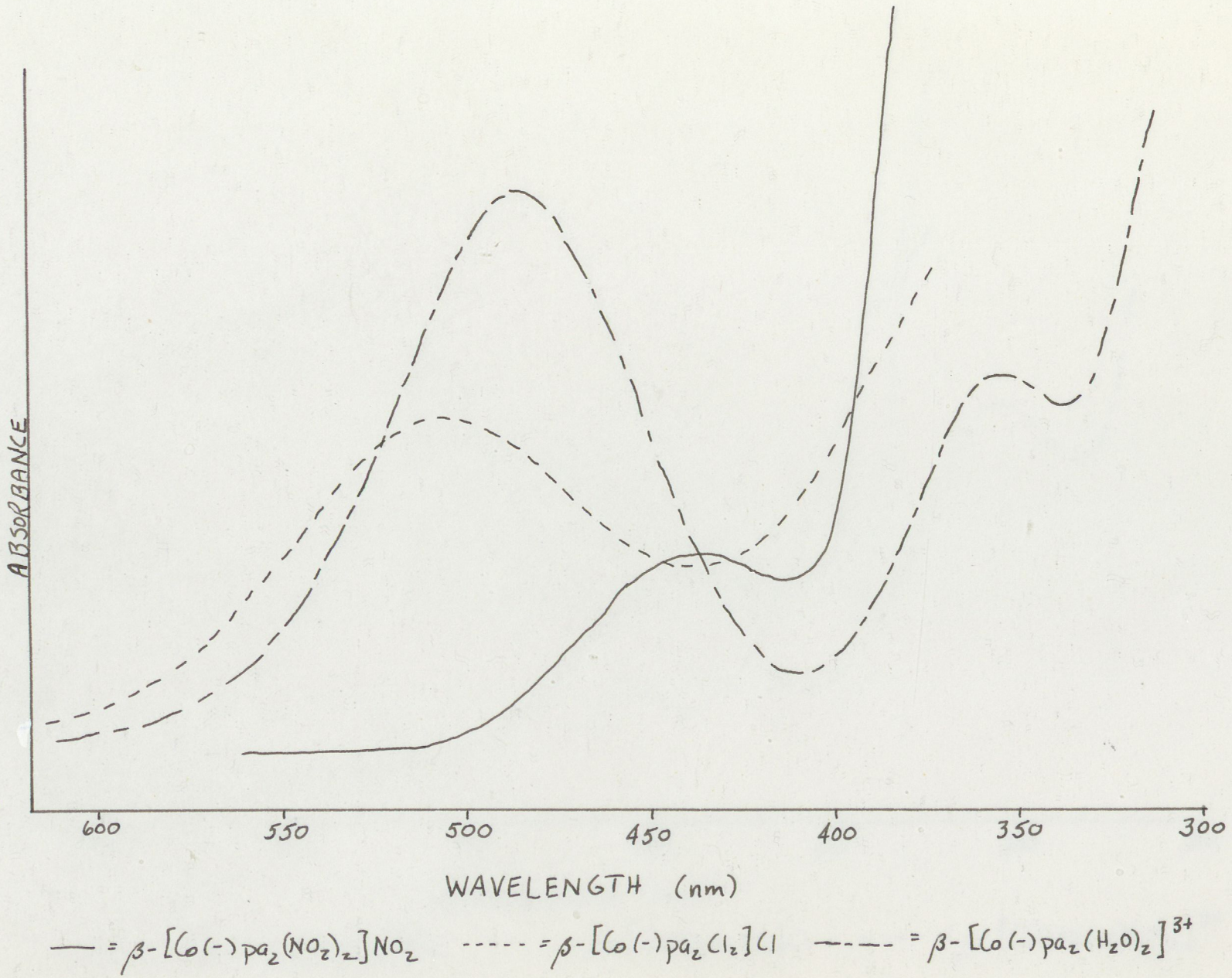
For the β-chloro isomer using the resolved ligand, the dot with high color intensity has the lower R_f value leading to the conclusion that the predominant product (presumably the D(--) isomer) has the slower elution time. This result is just the

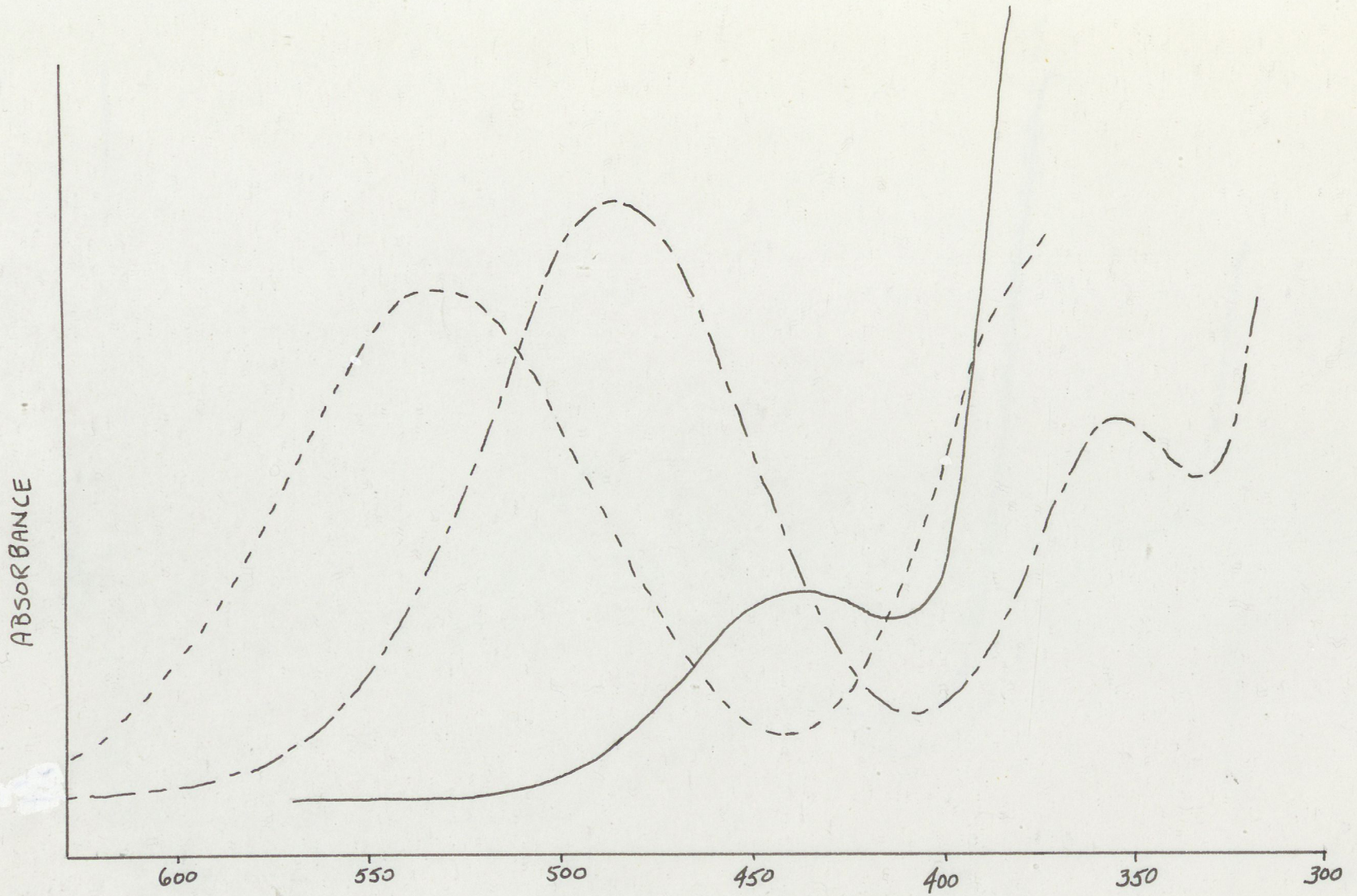
reverse of the observation for the aquo complex, but it can be rationalized as the effect of differing chemical structure on elution times.

To check these conclusions it would be necessary to do either ORD or CD measurements and attempt to correlate the signs of the Cotton effects with absolute configuration. If there is a large predominance of one configuration over the other it is possible a net effect will be observed. This, however, would not necessarily be proof, because there is no reason the diastereomers D(--) and L(--) should have the same absorbance. Some resolution should be attempted.

Conclusion: On the basis of chromatography it can be said there is stereoselectivity in the reactions of cobalt with the ligand 1-(2-pyridyl)ethylamine. Exactly what the equilibrium constant between the forms D(--) and L(--) is cannot be determined without further work involving resolution of the two isomers involved.

APPENDIX 1


ABSORBANCE
600
550
500
450
400
350
300
WAVELENGTH (nm)
— = β-[Co(-)pa$_2$(NO$_2$)$_2$]NO$_2$
----- = β-[Co(-)pa$_2$Cl$_2$]Cl
—--— = β-[Co(-)pa$_2$(H$_2$O)$_2$]$^{3+}$


ABSORBANCE
600
550
500
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400
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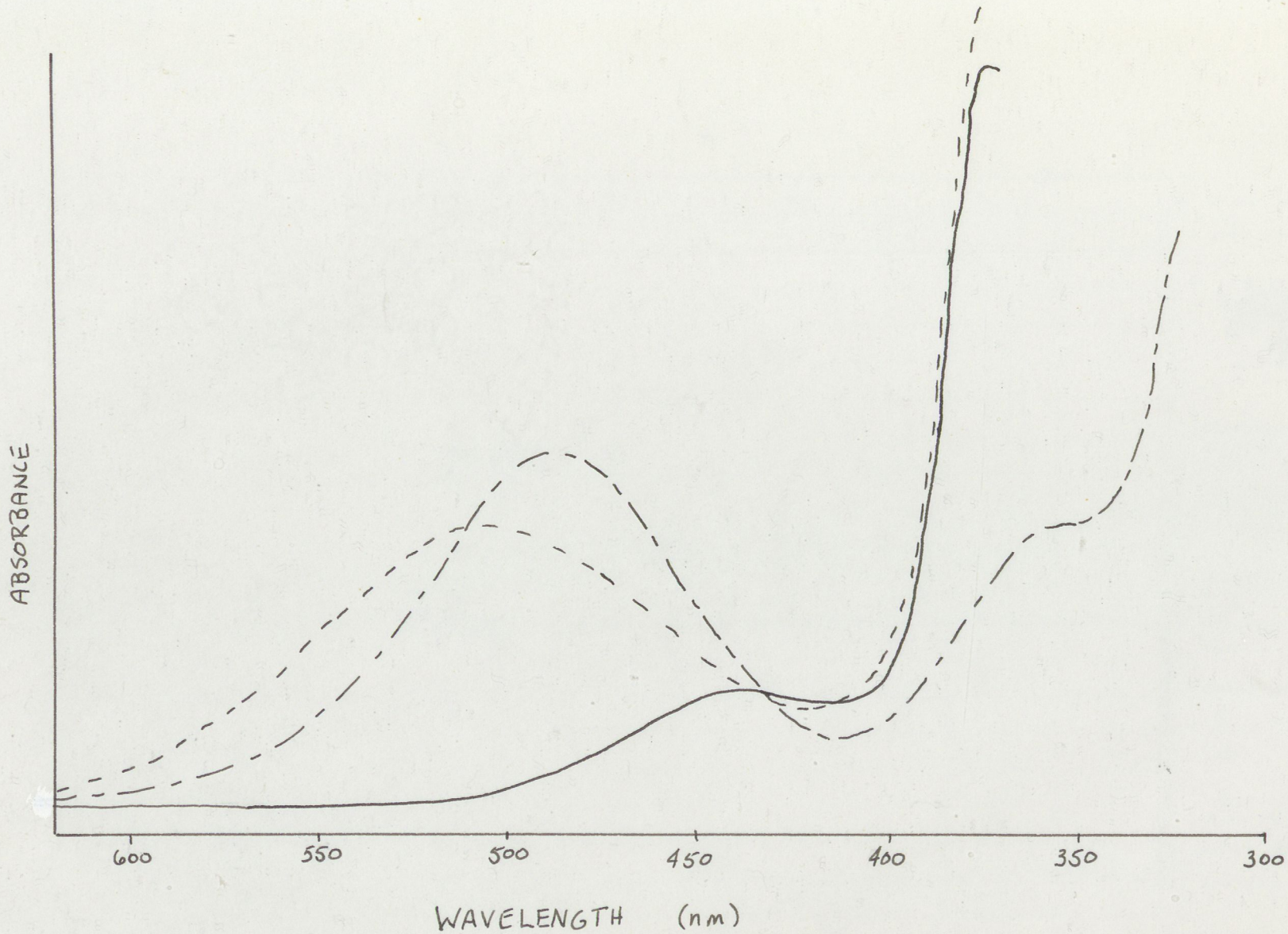
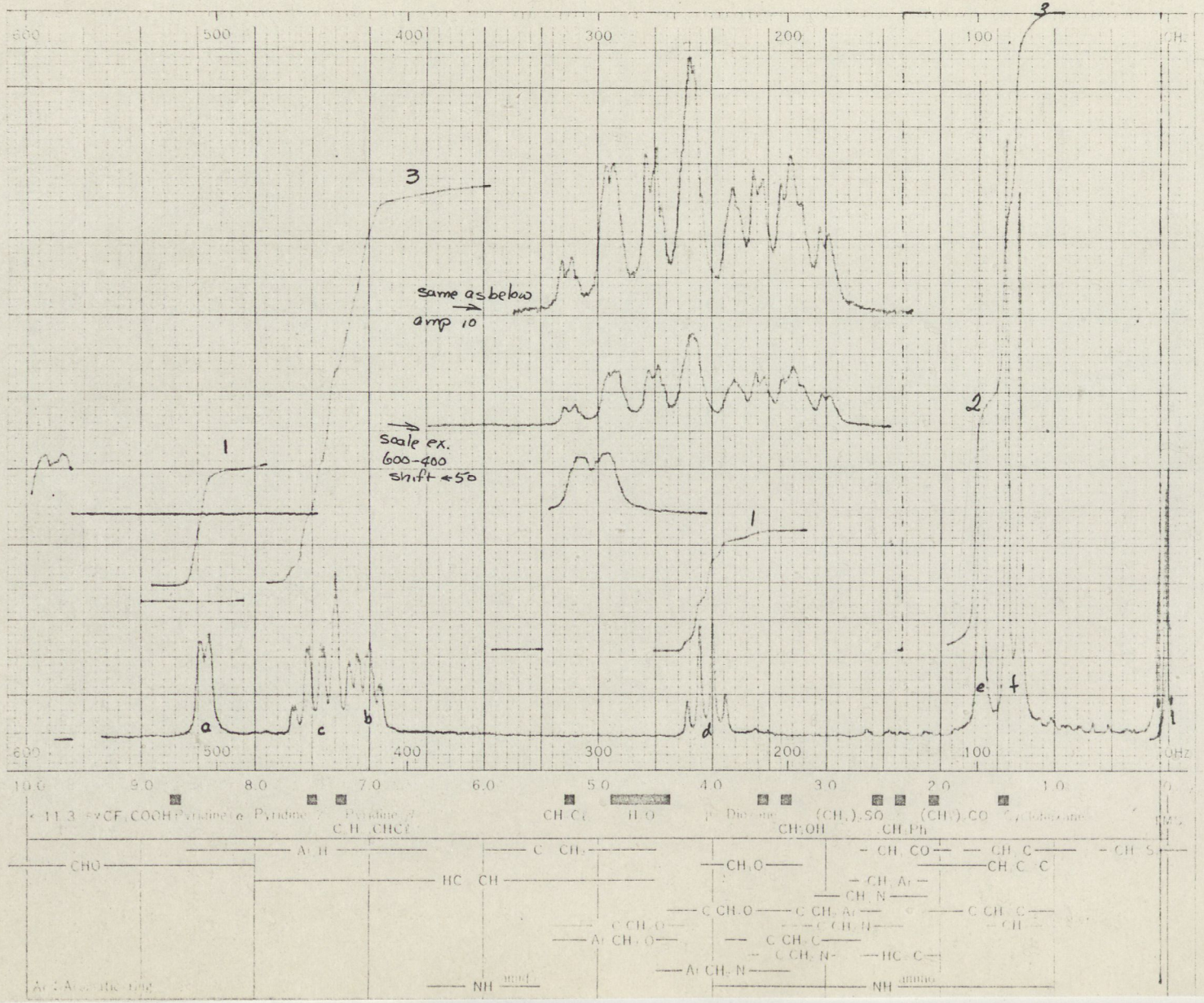
300
WAVELENGTH (nm)
—— = β-[Co(±)pa₂(NO₂)₂]NO₂
---- = β-[Co(±)pa₂Cl₂]Cl
—·— = β-[Co(±)pa₂(H₂O)₂]³⁺

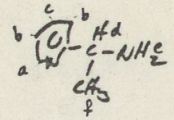


—— = α-[Co(±)pa$_2$(NO$_2$)$_2$]NO$_2$ ---- = α-[Co(±)pa$_2$Cl$_2$]Cl —·—· = α-[Co(±)pa$_2$(H$_2$O)$_2$]$^{3+}$



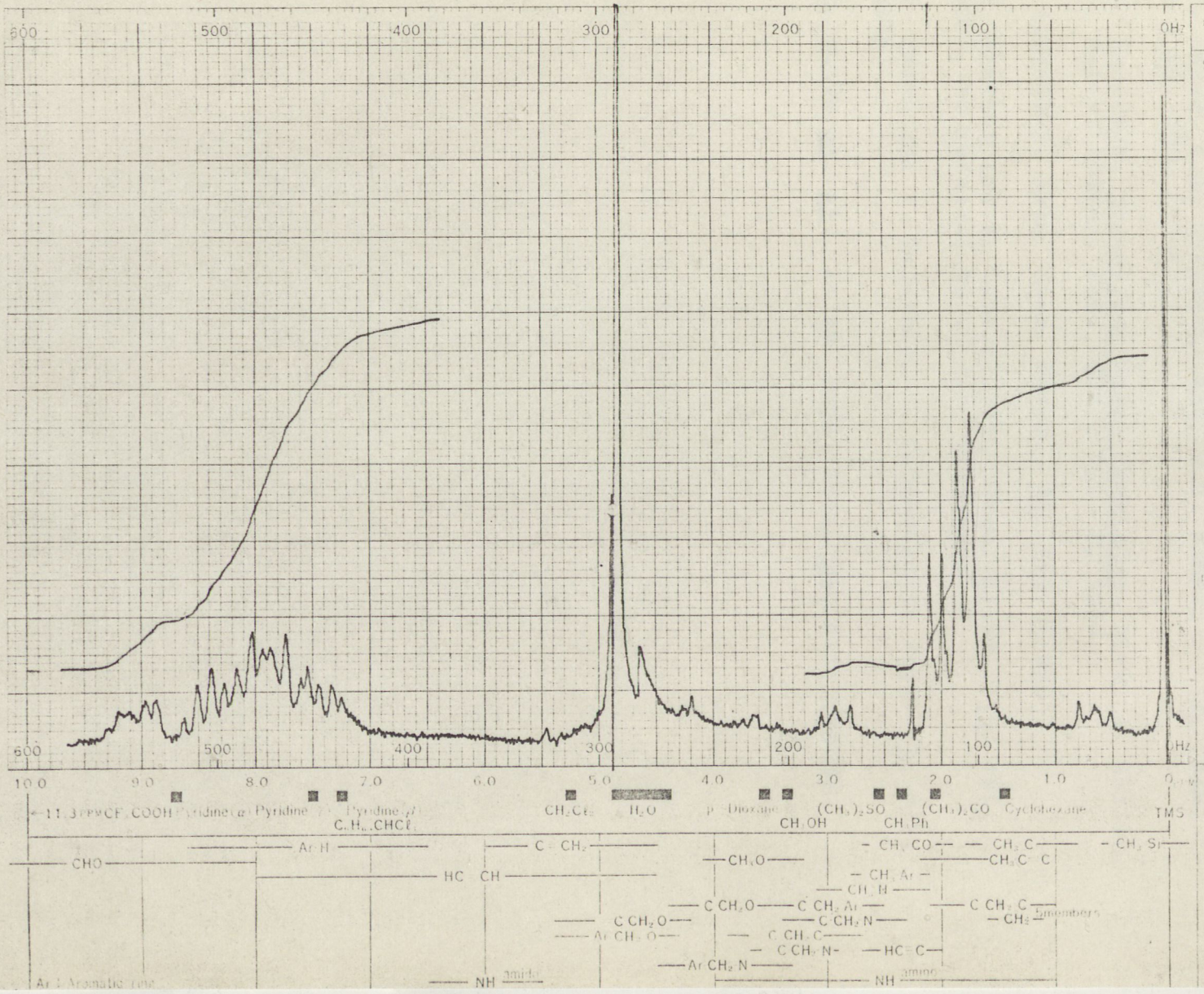
'H SPECTRUM NO. :

SAMPLE : 1-(2-pyridyl)-ethylamine



REFERENCE : TMS
SOLVENT : CCl_4
CONC : 50%
AMPLITUDE :
SPECTRUM : 7
INTEGRAL : 7
H₁ LEVEL : x
H₂ LEVEL :
GAIN : x
SWEEP WIDTH :
x
SHIFT :
SWEEP TIME :
x 300 150SEC SEC
DATE : 11/11/79
OPERATOR : RLW

REMARKS :



^{1}H SPECTRUM NO. :

SAMPLE : $[Co(pa)_2(H_2O)_2]$

β-isomer

REFERENCE : DSS
SOLVENT : D_2O
CONC :

AMPLITUDE :
SPECTRUM : 11
INTEGRAL : 9

H_1 LEVEL : X

H_2 LEVEL :

GAIN : X

SWEEP WIDTH : X

SHIFT :

SWEEP TIME : X 300/150SEC SEC

DATE : 1/22/75

OPERATOR : Rw

REMARKS : Large H_2O peak may obscure some other peaks. Try to move it with CF_3COOH. Phasing off?

21

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